on the freezer inclination and the volume of the liquid. With a different inclination of the freezer corresponds a different heat exchange surface which, therefore, can be changed according to the working conditions.

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Evaluation of Magnetic Basket Dissolution Apparatus I: Differences in Tablet Formulations

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Abstract □ The use of the magnetic basket dissolution apparatus as a means of following the dissolution of tablets was studied. Several different formulations of pentobarbituric acid tablets were manufactured and used to illustrate the ability of the magnetic basket dissolution apparatus to differentiate between the dissolution of tablets with differences in particle size of active ingredients, in formulation, and in hardness. The magnetic basket dissolution apparatus was compared with the USP XVIII and Levy beaker methods for following dissolution. Log probability plots were used as a means of providing a quick and accurate dimension for analyzing dissolution data.

Keyphrases □ Dissolution equipment—comparison of magnetic basket apparatus with compendial and Levy beaker methods for studying differences in tablet formulations □ Magnetic basket dissolution apparatus—differentiation between tablet formulations, compared with compendial and Levy beaker methods □ Tablet dissolution—magnetic basket apparatus used to study formulation differences, compared with compendial and Levy beaker methods □ Log probability plots—used to analyze dissolution data, magnetic basket apparatus compared with compendial and Levy beaker methods

In vitro dissolution profiles are of importance when they can be correlated to *in vivo* studies or when the results can be used to evaluate and examine relative differences in drug dissolution and, hence, availability for absorption between dosage forms or differences from batch to batch of the same formulation. Implied by these qualities is reproducibility of dissolution profiles for the dosage form and drug in question. An *in vitro* technique incorporating these capabilities is, of course, the ideal for which one strives.

In this quest, Levy and Hayes (1, 2) showed that the round-bottom beaker method in combination with slow agitation rates simulates, in physical appearance, the deposition of the dosage form in the stomach and mimics *in vivo* disintegration. In an earlier report (3), it was shown that the magnetic basket yielded reproducible dissolution results for both capsules and tablets. During the initial investigation of the magnetic basket, the concern was to ascertain the degree of reproducibility possible; in addition, it was found that certain characteristics of capsule disintegration and dissolution could be determined from the results. One type of tablet was examined, and it was determined that dissolution from this tablet could be reproducibly followed using the magnetic basket. No attempt at comparisons with other methods was made at that time.

This report delineates the reproducibility for dissolution of tablets, and it shows that the magnetic basket can be used to detect formulation differences in tablets. In this study, comparisons of the dissolution rate using the magnetic basket, the USP XVIII basket, and the Levy round-bottom beaker are discussed.

EXPERIMENTAL

Material—Pentobarbituric acid powder and pentobarbituric acid micronized were supplied by a commercial source[1]. The dissolution medium consisted of a buffer mixture (4) of hydrochloric acid and potassium chloride at pH 2. Fast flow lactose[2], microcrystalline cellulose[3], starch[4], and stearic acid[5] were purchased.

[1] Abbott Laboratories.
[2] Foremost Dairy, San Francisco, Calif.
[3] Avesil, FMS Corp., Newark, Del.
[4] Ruger Chemical Co., Inc., Irving, N. J.
[5] Fisher Chemicals, Fair Lawn, N. J.

Table I—Tablet Formulations

	Formula I	Formula II	Formula III	Formula IV
Pentobarbituric acid	—	—	25.0	25.0
Micronized pentobarbituric acid	25.0	25.0	—	—
Lactose	236.0	243.0	236.0	243.0
Microcrystalline cellulose	43.5	43.5	43.5	43.5
Starch	35.0	35.0	35.0	35.0
Stearic acid	10.5	3.5	10.5	3.5

Equipment—The three dissolution systems used included the USP XVIII dissolution apparatus (5), the round-bottom beaker (1, 2, 6), and the magnetic basket (3).

Tablets were compressed using a 16-station rotary tablet press[6] equipped with an induced die feeder. Standard concave punches, 0.95 cm. (0.37 in.), were used. A hardness tester[7] was employed.

Tablet Formulation—Tablets were compressed from the four formulations listed in Table I. All tablets were weighed and measured for thickness. Fifty percent of those tablets meeting specifications were examined for hardness; at least 75 tablets were examined for each hardness variation of all formulations.

Each of the four formulations was compressed at at least two hardnesses as determined by the hardness tester. For example, the range of hardness used for certain tablets was 8.6–9.0 with an average of 8.8; for softer tablets, a range was 3.1–4.0 with an average of 3.7.

Analysis of Tablets—The weight of each tablet was determined prior to dissolution, and the amount dissolved at any time t, reported as a percent of total acid, was determined at 240 nm. using appropriate blanks. Samples were taken at 2-min. intervals for the first 20 min. and then at 4-min. intervals until dissolution was complete. Reproducibility of results was determined by comparison of the variation produced at time intervals for similar tablets. For example, the Formula III tablets illustrated in Fig. 2 showed a standard error of the mean of 3.44, 5.07, 7.33, and 6.36 for the first four time intervals, respectively, with a reduction to 3.91 or less for the remaining samples. Each dissolution profile is the average of at least five tablets.

RESULTS AND DISCUSSION

Previous work (3) indicated that the magnetic basket could reproducibly follow the dissolution of both capsules and tablets. The additional versatility of this method can be seen if different formulations of the same drug are considered. In Fig. 1 the dissolution of tablets composed of Formulas III and IV are compared. By use of the magnetic basket method, differences between formulations that

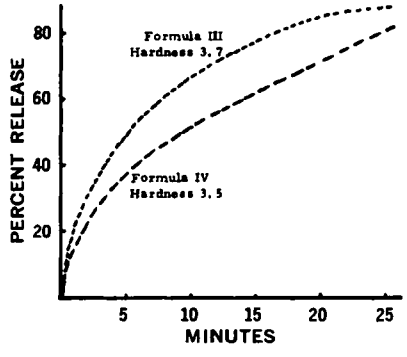

Figure 1—*Comparison of dissolution rates of active ingredients from tablets with different formulations and the same hardness, using the magnetic basket dissolution apparatus.*

[6] Model 216-RP Cherry-Burrell.
[7] Erweka Electronic.

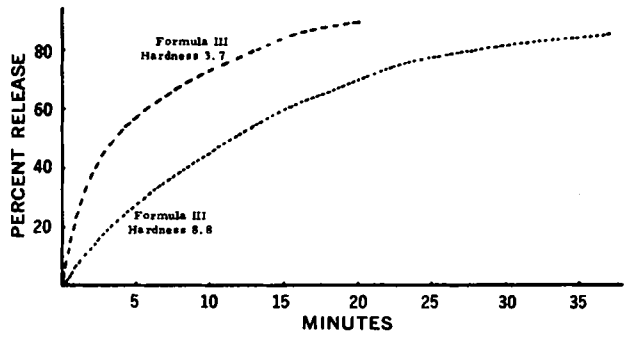

Figure 2—*Comparison of dissolution rate of active ingredients from tablets of the same formulation and different hardness, using the magnetic basket dissolution apparatus.*

are of the same average hardness and weight but differ in stearic acid content may be detected.

Figure 2 illustrates the difference found in dissolution between tablets using Formula III with different average hardnesses of 8.8 and 3.7. A distinct difference in the dissolution profiles of the two different hardnesses is seen, with the softer tablet as expected showing a much faster dissolution rate. The parallel dissolution behavior between the two tablets can be clearly seen using a log probability plot of time *versus* percent dissolved (7). Although the log probability relationship is most frequently used to describe the size distribution of particulate matter, it can be used in this case as a means of illustrating dissolution behavior. In the former case, both straight and curved lines may result. A straight line indicates that the sample examined is composed of a normal distribution, *i.e.*, all particles belong to the same population. A curved line indicates that the sample contains particles from more than one population. If the case of tablet dissolution is considered and the straight line is indicative of dissolution from a relatively unchanging set of parameters, then the correlation of dissolution behavior can be seen.

Figure 3 shows that two straight lines represent the dissolution profile of each tablet. It would seem that the first straight line is indicative of the initial dissolution–disintegration of the tablet when the tablet matrix is still present. That is, the surface area is relatively unchanged since the diminishing surface area of the tablet is offset by the increase in surface area due to disintegration. The second straight line should represent the dissolution phase when the tablet matrix is no longer present and dissolution is taking place from an infinite number of particles residing predominantly at the beaker bottom. Visual observation correlates with the appearance of the second linear segment in the log probability plots. Furthermore, in Wagner's (7) derivation of the rationale for use of log probability

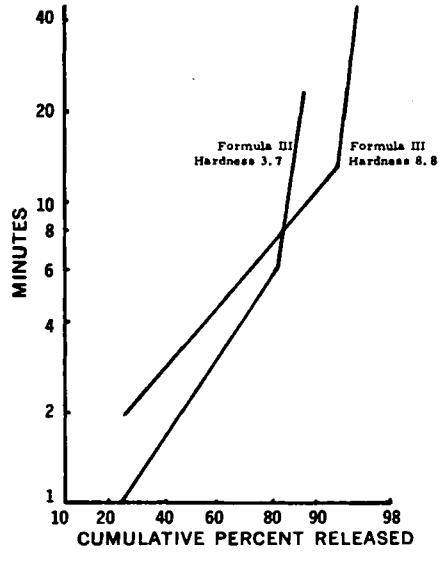

Figure 3—*Cumulative percent released* versus *time as an illustration of the treatment of data for tablets of the same formulation but of different hardness.*

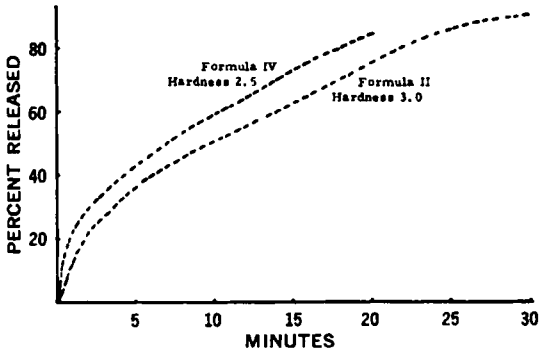

Figure 4—*Comparison of dissolution rates of active ingredient from tablets as a function of particle size of active ingredient, using the magnetic basket dissolution apparatus.*

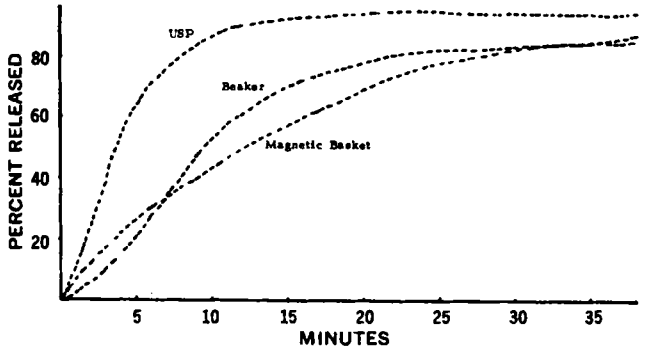

Figure 5—*Comparison of dissolution of active ingredient from tablets of the same formulation using the USP, beaker, and magnetic basket dissolution apparatus. All tablets were from Formula III with a hardness of 8.8.*

plots, his first assumption is that under sink conditions and changing surface area, one may assume that the surface area available for dissolution decreases exponentially with time. This would agree with the second segment of the straight line taking place after the tablet matrix has disintegrated.

One would expect deviation from the straight line concept in two places. The first deviation would be at the apex where the two straight lines intersect, since there is a transitional period when the dissolution–disintegration process and its concomitant "large" particles (small surface area) are changing to a pure dissolution process involving many smaller particles with a large surface area. The second deviation would be at the end of the second straight line when the material is approaching 100% dissolution. Here one is on the plateau of the regular dissolution curve, and the amount of drug dissolving per unit time is somewhat less than that rate witnessed during the initial portions of the second straight line. Therefore, the cumulative percent dissolved would remain virtually unchanged as time increased, giving rise to almost a vertical line. This deviation is small in this case and, although not shown in Fig. 3, may be attributed to a discontinuance of exponential exposure of the particle surface due to an increased shielding of the drug particle by insoluble tablet ingredients. The difference in hardness between the two tablets is readily seen by comparison of the intercepts of the two straight lines. For the tablets with an average hardness of 3.7, this intercept occurs at 6 min. The harder tablets, with an average hardness of 8.8, show this intercept at 13 min., which is what would be expected of a higher compression tablet.

To illustrate the ability of the magnetic basket to differentiate between tablets with different particle size of the active ingredient, Formulations II and IV were used. Formulation II contained micronized pentobarbituric acid, with a mean surface diameter of 4.42 μ; in Formulation IV, the pentobarbituric acid had a mean surface diameter of 9.96 μ. Figure 4 shows the dissolution profiles for these two formulations using tablets of comparable hardness. While the magnetic basket shows a difference between the dissolution profile as a function of particle size, the micronization of pentobarbituric acid does not give faster dissolution. This behavior was also shown to be true when comparing Formulations I and III.

Figure 5 shows a comparison of the official USP XVIII dissolution test, the Levy beaker method, and the magnetic basket method using tablets from Formulation III with an average hardness of 8.8. All three methods show similar dissolution profiles, with the USP method reaching its peak dissolution somewhat faster than the other two methods. A factor that would contribute to faster dissolution rates using the USP XVIII apparatus is the obvious screening, through centrifugal force, imposed on the dosage form placed in the spinning basket. This spinning and resulting rapid dissolution also tends to mask or level relatively small differences in tablet dissolution rates. The Levy beaker and the magnetic basket methods showed similarity in all dissolution comparisons of the various formulations.

While in a previous preliminary study there were indications that reproducibility and detection of formulation differences in both capsules and tablets were possible with the magnetic basket, it may be concluded from this study that the magnetic basket method is versatile in its ability to differentiate between the common parameters of hardness, particle size, and formulation differences found in these tablet studies. Furthermore, it will apparently provide a means of differentiation for both capsules and tablets, presenting the results in a directly comparable manner. Its use in combination with log probability plots provides a quick and accurate means of analyzing dissolution data.

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